

Original Research Article

Postoperative stroke in head and neck cancer patients submitted to surgery

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ABSTRACT

Background: Stroke is a highly morbid complication after head and neck surgery (HNS). Our purpose was to report the casuistic of postoperative stroke (POS) in ENT Department of Oporto Cancer Institute, discuss predictable causes and prognosis.

Methods: Retrospective study that included cases of POS in our Department, between 2012 and 2017. Medical files were reviewed and perioperative aspects were analysed.

Results: We identified 8 cases of POS in 293 HNS performed. All underwent to HNS including bilateral ND as primary treatment. Several cardiovascular risk factors (CVRF) were present, especially carotid artery stenosis (CAS). Complete internal carotid artery (ICA) encasement was present in 2 patients, in whom artery ligation was performed. Acute drop of bispectral index (BIS) occurred in 1 patient. Stroke occurred at 2.8 post-operative day (in mean) and was ischemic in 7 patients and haemorrhagic in 1. The most affected vessel was cerebral media artery (87.5%). Hemiparesis was the main clinical manifestation (63%). Incidence of POS was 2.7%. Functional and neurologic recovery occurred in 50%. Mortality rate was 37.5%.

Conclusions: Our findings suggest that worst outcomes were observed in patients with advanced tumour stages, vessel tumour involvement or carotid artery stenosis presence with requirement ligation of ICA, higher number of CVRF, and low or sudden decrease in BIS values during surgery. According to our results we recommend to screen, select and optimize patients to minimise the incidence and severity of this complication.

Keywords: Head and neck cancer, Head and neck surgery, Stroke, Thrombogenesis

INTRODUCTION

Postoperative stroke (POS) is characterized as an ischemic or haemorrhagic cerebrovascular event with motor, sensory or cognitive neurologic signs that persists for more than 24 hours and occurs within 30 days after surgery.¹

Stroke after head and neck surgery (HNS) is a potentially devastating complication that increases morbidity and mortality.²

Available literature reports an incidence of stroke after HNS including with neck dissection (ND) ranging from 3.2% to 4.8%. These values are well above from the estimated for non-head and neck surgeries (0.05 to 0.2%).²

Surgery that involves significant manipulation of the carotid artery is well established to be associated with an increased risk of POS. HNS with ND also involves significant carotid artery manipulation and is generally performed in a population of patients with several

cardiovascular risk factors (CVRF) and with increased risk for carotid artery stenosis (CAS).³

Patients submitted do HNS including ND may also experiment intraoperative problems like severe hypotension, hemodynamic instability, considerable blood losses, neck incorrect positioning with extension and rotation and, prolonged surgical procedures.

These conditions have been associated with increased risk of POS in head and neck cancer (HNC) patients submitted to surgery.¹⁻⁴

So, it's important to evaluate and understand patient-related, surgical, anaesthetic, preoperative and intraoperative conditions that may predispose or increase the risk for POS after HNS.

The combination of preoperative screening with identification of the potentially controllable risk factors, and optimization of surgical and anaesthetic techniques, may provide useful tools to reduce short-term morbidity and mortality related with this complication.

The aim of the present study is to report the casuistic of POS in our Department and analyse predictable causes and patient prognosis.

METHODS

We conducted a retrospective study with descriptive analysis of the data. Between January 2012 and April

2017, 293 HNS including bilateral ND were performed in our Department. POS was identified in 8 patients. These cases were reviewed and all information was obtained by consulting medical reports.

All patients included had clinical and histological diagnose of HNC, were submitted to HNS with bilateral ND as primary treatment option and had POS confirmed by neurological physician evaluation, supported by imaging studies as computed tomography (CT) or magnetic resonance imaging (MRI).

The following variables were analysed: patient's demographics, medical and surgical history, CVRF, previous cerebral or cardiovascular events, adjuvant or neo-adjuvant treatments, primary tumour location and stage, type and details of surgery, intraoperative findings, intraoperative conditions [average of blood pressure, blood losses, need of red blood cells' (RBC) transfusion, values and variation of bispectral index (BIS), surgery duration], stroke features and evolution.

RESULTS

From January 2012 to April 2017, a total of 293 HNS including ND were performed in our Department. During this period, a total of 8 cases of POS were identified. In our series, POS incidence was 2.7%.

Sample was composed by 8 caucasians male patients, with an average of 59.8 years old (SD±6.7).

Table 1: Patient's medical, surgical and stroke history.

Patient	Age	Sex	Primary tumor location and stage	Surgery	CVRF	Infarction territory and stroke mechanism	PO day of stroke	Clinic presentation	Evolution
1	61	M	Larynx (Transglottic) T4aN3M0	TL+MRND+ hemitiroidectomy + partial parotidectomy ----- Ligation of right ECA and IJV	Alcohol Smoke HBP CHF	RCMA Embolic	Day 2	Left hemiparesis Anosognosia	Favourable clinic evolution Partial recovery of neurologic deficits
2	52	M	Larynx (Supraglottic) T4aN1M0 + Oropharynx (Posterior wall) T2N0M0	TL + SND + pharyngectomy (partial)	Alcohol Smoke Dyslipidemia	RCMA Embolic	Day 2	Pyramidal and Horner Syndromes	Favourable clinic evolution Partial recovery of neurologic deficits
3	64	M	Larynx (Glottic) T4aN2bM0	TL + SND + Tiroidectomy	Alcohol Smoke HBP CAS DM2	LCMA Embolic	Day 6	Cardiorespiratory arrest Anoxic coma	Dead D8 Post Surgery
4	57	M	Hypopharynx (Piriform sinus) T3N2cM0	TL + SND	Alcohol Smoke CAS PAD LC	LCMA Embolic	Day 3	Right hemiparesis	Multiple neurologic deficits

Patient	Age	Sex	Primary tumor location and stage	Surgery	CVRF	Infarction territory and stroke mechanism	PO day of stroke	Clinic presentation	Evolution
5	71	M	Oropharynx, (Palatine tonsil) T3N2bM0	COMMANDO + MRND + PMM flap + tracheostomy	Alcohol Smoke PAD	Unknown artery Haemorrhagic	Day 4	Right hemiparesis and hypoesthesia	Favourable clinic evolution Partial recovery of neurologic deficits
6	59	M	Larynx (Supraglottic) T4bN2cM0	Laser epiglottectomy + SND ----- Encasement of right CA Ligation of right ICA	Alcohol Smoke HBP CAS PAD DM2 AF CPOD	RCMA Embolic	Day 2	Cardiorespiratory arrest Anoxic coma	Dead D8 Post Surgery
7	49	M	Larynx (Supraglottic) T4aN2cM0	TL + MRND ----- Ligation of bilateral IJV	Alcohol Smoke HBP	RCMA Embolic	Day 3	Left hemiparesis	Favourable clinic evolution Partial recovery of neurologic deficits
8	65	M	Oropharynx (Uvula) T4bN3M0	Left pharyngectomy + RND + parotidectomy + PMM flap ----- Encasement of left CA Ligation of left ICA and IJV	Alcohol Smoke CAS PAD Dyslipidemia	LCMA Thrombogenic	Day 1	Initial tetraparesis with evolution to right hemiparesis	Dead D10 Post Surgery

AF: Arterial Fibrillation; CA: Carotid Artery; CAS: Carotid Artery Stenosis; CHF: Congestive Heart Failure; COMMANDO: Combined Mandibulectomy and Neck Dissection Operation; CPOD: Chronic Pulmonary Obstructive Disease; DM2: Diabetes Mellitus type 2; ECA: External Carotid Artery; ICA: Internal Carotid Artery ; HBP: High Blood Pressure; IJV: Internal Jugular Vein ; LC: Liver Cirrhosis; LCMA: Left Cerebral Media Artery; MRND: Modified Radical Neck Dissection; PAD: Peripheral Artery Disease; PMM: Pectoralis Major Myocutaneous; PO: Postoperative; RCMA: Right Cerebral Media Artery; RND: Radical Neck Dissection; SND: Selective Neck Dissection; TL: Total Laryngectomy.

Table 2: Patient’s intraoperative conditions.

Patient	Intraoperative BP (average)	Intraoperative BL	Blood Transfusion	Surgery duration	BIS		Sudden decrease (after induction)
					Range	Average	
1	85/40 mmHg	1000 cc	1 RBCU	3h 45min	31-98	46	No
2	100/60 mmHg	750 cc	None	3h 20 min	33-97	48	No
3	80/50 mmHg Periods of 50/35 mmHg Adrenergic support	500 cc	None	4h 30 min	22-88	43	Yes
4	80/40 mmHg	1000 cc	2 RBCU	4h	27-91	38	No
5	130/90 mmHg	600 cc	None	3h 30 min	36-98	45	No
6	70/30 mmHg Severe hypotension Adrenergic, crystalloids and colloids support	500 cc	None	3h 10 min	23-97	38	No
7	90/65 mmHg	1200 cc	None	4h 20 min	32-98	45	No
8	80/35 mmHg Severe hypotension Adrenergic, crystalloids and colloids support	650 cc	5 RBCU	6h	27-98	52	No

BIS- Bispectral Index; BP – Blood Pressure; BL – Blood Losses; RBCU– Red Blood Cells Units.

All the studied patients had cardiovascular and stroke risk factors analysed, with a maximum of 8 and a minimum of 3 risk factors for patient (Table 1). Smoke and alcohol consumption were present in all of them. Most prevalent comorbidities, present in 50% of patients, were high blood pressure (HBP), peripheral artery disease (PAD) and CAS suggested by CT and MRI and properly accessed by doppler ultrasonography. No one of the patients had previous stroke history, transitory heart attack neither previous adjuvant or neo adjuvant treatments.

Primary tumour was localized in laryngopharynx in 5 patients, oropharynx in 2, oropharynx/laryngopharynx in 1. All underwent to surgery including bilateral ND as primary treatment.

Internal carotid artery (ICA) encasement was observed in 2 patients, in whom ligation by necessity of this vessel was performed. External carotid artery (ECA) ligation was performed in 1 patient. Internal jugular vein (IJV) ligation was performed in 3 patients. Intraoperative hypotension (IOH) is defined as more than 10 minutes period of systolic blood pressure less than 80 mmHg.⁸ It occurred in 4 patients and was severe in 3. Blood losses (BL) were in mean 775 mL, with RBC transfusion required in 3 patients. BIS values were 44 in average (ranged between 22 and 98) and sudden decrease during surgery occurred in 1 patient. Surgery duration was in mean 4 hours.

Strokes were identified in mean at 2.8 post-operative day, having been ischemic in 7 patients (embolic in 6 patients and thrombogenic in 1 patient) and haemorrhagic in 1 patient. The most affected artery was cerebral media (87.5%) and hemiparesis was the main clinical manifestation (63%).

Functional and partial neurologic recovery occurred in 4 patients (50%). Impaired function with multiple neurologic deficits was observed in 1 patient (12.5%). Dead occurred in 3 patients, 8.7 days after surgery in mean. Mortality rate was 37.5%.

Surgery details, intraoperative findings, CVRF, stroke features and evolution are summarized in Table 1. Intraoperative conditions are summarized in Table 2.

DISCUSSION

In this study, we analyse the incidence of individual, surgical and intraoperative conditions that may increase the risk of POS in patients with HNC submitted to HNS including ND. We identify the most predictable causes associated with POS, and compare our results with published data about this topic.

In the literature, POS rates after HNS including ND are unclear and wide ranging, being estimated between 0.2 and 4.8%. In early nineties, Nosan et al and Rechtweg et

al, reported a significantly elevated risk of stroke after HNS including ND (4.8% and 3.2% respectively).^{4,5} More recently, Thompson et al and MacNeil et al, reported lower risks (0.2% and 0.7% respectively) and the authors considered that these results can be related with larger samples and higher level of evidence from case series.^{2,3} In our series POS incidence was 2.7%, which is in accordance with the range of most published data.

In consulted series, more than 80% of recognized POS were identified until the 10th post-operative day.⁴ In our series, POS was diagnosed in mean at 2.8th day after surgery, which can be related with the diagnostic techniques available nowadays, better vigilant attitudes in Intensive Care Units and, prompt and high index of discrimination of exams.

Cramer et al, calculated the risk of POS in patients undergoing ND in a large multi-institutional outcomes database.¹ They found that among patients with established CAS or at higher risk, ND was associated with an increased risk of POS. This supports the hypothesis that manipulation of the atherosclerotic carotid arteries is presumably a strong risk factor for POS.

Thompson et al, discussed risk factors for stroke associated with ND in patients with HNC, and considered that CAS is the single most important risk factor for stroke.⁶ CAS is related with several risk factors like HBP, PAD, diabetes, smoking, male gender, advanced age and external radiotherapy for head and neck cancer. Patients with HNC usually have many of these conditions that make them more susceptible to POS. In our series, 50% of patients had CAS, suggested by preoperative CT and MRI findings of ICA calcification and stenosis, promptly documented and classified by Doppler ultrasonography before surgery.

We cannot exclude that the remaining 50% did not have CAS once they had several risk factors, as mentioned above. In fact, they can have asymptomatic CAS or complaints never mentioned to doctors to motivate further studies.

Our sample included 2 patients (patient 6 and 8) with intraoperative findings of ICA tumour encasement in which ICA ligation was performed. These patients had extensive strokes, ipsilateral to the ligated ICA that culminated in dead. Tumour invasion of carotid arteries is a technical requirement for head and neck surgeons. Carotid wall invasion most often arises from direct extension of a primary HNC of hypopharynx or from bulky jugular chain lymph node metastasis with extracapsular extension. These patients may be selectively considered for carotid resection as part of primary surgical treatment or a salvage attempt after prior radiotherapy and chemotherapy.⁷

Recent series advocate selective use of carotid resection as part of primary surgical therapy for HNC. Results from these series suggest better disease-free survival with carotid resection than with nonsurgical therapies in previously untreated patients. When resection of the carotid artery as part of HNS is considered, preoperative evaluation can identify which patients are at greatest risk for neurologic sequels, and carotid reconstruction must be considered whenever possible to decrease the risk of such complications. Sometimes, in cases of carotid blowout, emergent carotid ligation and/or resection may be needed, without any preoperative testing. In this scenario, reconstruction is still favourable whenever possible, although sometimes it may be impractical. Unfortunately, even with reconstruction, patients still carry some risk of immediate and delayed neurologic sequels from the procedure.⁷

The most widely proposed mechanism for POS is arterial ischemia, which agrees with our results once 7 strokes were ischemic (6 were embolic and 1 was thrombogenic). Nosan et al and Thompson et al, both consider that ND and vascular manipulation increase the risk for POS than non-neck procedures due to the high incidence of CAS and neck difficult positioning during surgery in these patients.⁴⁻⁶ Neck is often hyper extended and rotated for long periods, which may cause intimal tearing of carotid artery, thrombus formation or plaque ulceration associated to turbulent flow. Also, carotid artery is often retracted and this has the potential to dislodge pre-existent thrombus or plaque.

Hypo perfusion is often mentioned as a possible cause for POS. We didn't find specific literature that correlates intraoperative hypotension (IOH) with POS in HNS. Bliker et al, made a review about the role of hypotension in perioperative stroke.⁸⁻⁹ They founded that hypotension contributes as a primary factor or more frequently as a secondary factor for development of perioperative stroke and considered that many other factors may contribute to the pathophysiology of these events.⁹ Unusually low blood pressure will eventually result in neurological damage, however, the threshold and duration concerning which an association might be found have not been well investigated. Thus, the exact role of IOH in POS remains unknown. In our data, 4 patients experienced IOH that was severe in 3. Curiously, 3 of them died and 1 had an unfavourable evolution with multiple neurologic deficits. However, these worst outcomes can be attributable to other variables present in these patients as a higher number of CVRF and greater tumour stages.

BIS is normally used to monitor depth of anaesthesia and it can also be used to detect hypo perfusion states during surgery. Many articles have already described the use of BIS as a possible marker of cerebral hypo-perfusion.¹⁰ Values between 40 and 60 indicate appropriate anaesthesia levels. In our results, the average of BIS values was 44. However, the patient 3 experienced a sudden decrease of BIS values during surgery and patient

4 had average values under 40. The first one mentioned had an extensive stroke with cardio respiratory arrest, anoxic coma and died at 8th postoperative day. The second one also had an extensive stroke with unfavourable evolution which resulted in multiple neurologic deficits. These worse outcomes can be associated to decrease in brain activity, hypo perfusion and anoxia due to less cerebral metabolism which leads to changes in electroencephalogram and hence in BIS values.

In our series, 3 patients have died after POS, 2 of them with intraoperative findings of ICA encasement having been submitted to ICA ligation and 1 had clear and documented BIS drop values during surgery. All of them had in common several CVRF and particularly CAS accessed by Doppler ultrasound. Within the other 5 patients of our series, 4 had a favourable evolution and 1 remain with multiple neurologic deficits after stroke. This last patient had CAS and BIS mean values under the recommended during surgery.

Our findings should be interpreted with several limitations in mind. First, our sample is short because POS is a low prevalent entity, so the results cannot be securely extrapolated to general HNC patients who perform HNS including ND. Second, the surgeries were not effectuated by the same surgeon and/or anaesthetist, which impose condition variability. Finally, we analyse the rate of strokes that presented with gross neurologic deficits, but we could have missed strokes that had only subclinical manifestations.

CONCLUSION

Our findings suggest that worst surgical outcomes are related to more advanced tumour stages, malignant involvement with ligation of ICA, higher number of CVRF, especially if CAS was present, and low or sudden decrease in BIS values during surgery. IOH has an unknown and unpredictable role, being most probably related to neurological damage than with stroke fatality.

We aimed to emphasize the importance of preoperative screening, optimization of intra operative conditions and attentiveness to any neurologic change in the immediate postoperative period.

To minimise the incidence and severity of these complications, it's important to make careful preoperative studies, optimize patient's CVRF, also as surgical and anaesthetic conditions.

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